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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,699	KANO ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- Th MAILING DATE of this communication appears on the cov r sh t with th correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9,11-20,24,26,28-33,37,39 and 41-61* is/are pending in the application.

4a) Of the above claim(s) *46-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/19/04* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 19, 2004 has been entered.

The amendment and response filed with the request have been entered. Claims 1, 11-13, 16, 17, 20, 28, 29, 33, 41, 42 have been amended.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 11/19/04 response would be addressed to the extent that they apply to current rejection.

Election/Restrictions

Applicants request to include claims 46-61 upon allowance of this application because the patentably distinct species set forth in claims 46-61 are sufficiently related such that no serious burden would be imposed upon the Office, and since a reasonable number of additional species should be considered in an allowed generic claim.

In response, it is noted that the original claims explicitly presented a V gene defective and implicitly a V gene intact species, thus, there is no action on restriction. It

is also noted that numerous forms of mutations targeting different genes of a sendai virus or derived vectors are abundant in the art, such as the C, N, L, and P protein mutation in addition to the V and F gene mutation/deletion (e.g. Hu et al, Virology. 1999 Oct 10;263(1):195-208; and Gotoh et al, FEBS Lett. 1999 Oct 8;459(2):205-10; USP 6,828,138). These are structurally distinct and mutually exclusive sendai viral vectors, given the rebuttable presumption that viral vectors that are not similar in structure are not presumed to function similarly, the claimed vectors are expected to have different physiological properties, and different modes of action, such as different infectivity and levels of heterologous gene expression, and thus different biological different effects (MPEP 806.04, 808.01). Hence, recombinant sendai viral vectors with different gene mutations require distinct search criteria and technical considerations. Additionally, considering the level of skill in the art, it does not appear that the vectors deficient in V gene would have been obvious over the vectors deficient in F gene. The search and examination of different sendai viral vectors may have certain overlap, but they are not co-extensive. In view of the amount of literature in today's patent and non-patent databases, examining groups drawn to different gene mutations together would have imposed a serious search burden on the Office. Accordingly, only the recombinant sendai virus vector without a V gene deletion will be considered as the reasonable additional species, and will be addressed in this Office action. The subsequent amendment should reflect such restriction.

Therefore, it is maintained that these inventions or species of inventions are distinct due to their divergent subject matter. Further search of these inventions is not

co-extensive, as indicated by the separate search criteria. The requirement is still deemed proper and is therefore made **FINAL**.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-61 are pending, however, claims 46-61 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45 are under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings, or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement;* Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

These claims are directed to a sendai viral vector encoding proteins of an immunodeficiency virus, or *a part of a protein* such as a part of the SIVgag protein. Given the broadest reasonable interpretation, the claims encompass any recited proteins of claim 1, and any portion of the protein. However, the specification fails to provide an adequate written description for the structural-function of the part of the protein, i.e. what part of the protein such as recited in claim 1 would have sufficient antigenecity so that a protective immune response could be induced. Accordingly, the specification fails to provide an adequate written description for what is now claimed.

It is well known in the art, the immunogenecity of a given protein is very much associated with its sequence and 3-D structure, and further determined by the antigen

processing and presentation process. As known in protein structure and function, any change in amino acid sequence of an antigen may affect its 3-D structure, and subsequently antigen processing and presentation, and the ability to induce an immune response. In analyzing whether the written description requirement is met for the claimed subject matter i.e. a genus of HIV/SIV proteins including full-length or a portion of the protein, a representative number of species is needed by the distinguishing and other relevant identifying characteristics, such as the ability to induce a protective cellular immune response. However, the only disclosed species having the ability to induce a protective cellular immune response is the full-length *gag* protein; the specification fails to disclose one single species that is a part of the proteins as recited and has the ability to induce a protective cellular immune response. In fact, a post-filing date publication (*Matano et al*, AIDS. 2003 Jun 13;17(9):1392-4) evidenced that a full-length *tat* protein can not induce or enhance a protective immune response as compared to V(-)Sev-SIV-gag, thus V(-)Sev-SIV-tat would not have been served as a vaccine. In view of such, the specification fails to provide an adequate written description for the function of the proteins and parts of the proteins of an immunodeficiency virus as listed in claim 1.

An adequate written description for a protein requires more than a mere statement that it is part of the invention; what is required is a description of the structure and function of the protein and the part itself. With respect to the method claims, adequate description of the methods first requires an adequate description of the materials, which provide the means for practicing the invention.

The Revised Interim Guidelines state "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (Column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (Column 2, page 71436).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION *OF THE INVENTION*. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, *WHATEVER IS NOW CLAIMED.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of or representative species of genus

that could be used for vaccination. Therefore, only the described V(-)SeV/SIV-Gag meets the written description provision of 35 U.S.C. §112, first paragraph.

To the extent that the claimed methods are not described in the instant disclosure, claims 1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described that is not conventional in the art.

These claims are drawn to a protein of a HIV/SIV that is capable of inducing a protective immune response, however, as indicated *supra* in the written description section, the specification fails to provide an adequate description for the broad classes of proteins encompassed by the claims. Since the disclosure fails to describe the common attributes or characteristics that identify members of the claimed genus, a SIV-Gag alone is insufficient to describe the genus. One cannot extrapolate the teachings of the specification to the scope of the claims because the skilled artisan cannot envision the detailed structures of active agents encompassed by these claims, thus would not know how to use the invention without first carrying out undue experimentation to determine which of the agents would have the recited function. Therefore, in view of the limited guidance, the lack of predictability of the art, and the breadth of the claims, one

skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

Claims 1-5, 7, 9, 16-20, 24, 26, 28-33, 37, 39, 41-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a mutant sendai virus vector defective of V gene (*V*-) and expressing a Gag protein of an immunodeficiency virus, and intranasally administering such to a subject for vaccination, and optionally boost with a *plasmid* DNA encoding a *Gag* protein by intradermal gene gun, does not reasonably provide enablement for intranasally administering a sendai viral vector without V gene deletion (SeV) expressing any protein of an immunodeficiency virus and obtaining a vaccination effect. The specification does not reasonably provide enablement for using a V(-) sendai viral vector encoding any protein as listed in claim 1 as a *vaccine*, and it does not provide enablement for boosting with any DNA vector or encoding the genome of an immunodeficiency virus, and administering such by any route of administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir.1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the

art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the scope of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

Claim 1 starts with "a vaccine comprising...", claim 5 reads "a method for vaccination", claim 20 recites "a method for inducing a cellular immune response specific to a virus protein of an immunodeficiency virus in an animal", and claim 17 requires the composition induces a cellular immune response specific to the Gag protein or the part of it. These claims clearly or implicitly state the intended use of the composition and methods. With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. "DURING PATENT EXAMINATION, THE PENDING CLAIMS MUST BE 'GIVEN THEIR BROADEST REASONABLE INTERPRETATION CONSISTENT WITH THE SPECIFICATION'. *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 Fed. Cir. 2000" (MPEP 2111). "WHEN A COMPOUND OR COMPOSITION CLAIM IS LIMITED BY A PARTICULAR USE, ENABLEMENT OF THAT CLAIM SHOULD BE EVALUATED BASED ON THAT USE". (MPEP 2164.01c) When analyzing the enabled scope of the claims, the intended use is to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. "A vaccine composition" is defined as a composition for therapeutic use, to prevent, alleviate, treat, or cure a disease within the animal to which the substance is administered, therefore, will be evaluated by the standard. As such, the

broadest reasonable interpretation of the claimed invention properly encompasses genetic vaccination for an immunodeficiency virus, therefore, the claims will be evaluated by that standard.

The claims are drawn to a method for vaccination using recombinant virus vector. The specification teaches the creation of a mutant sendai virus, V(-)SeV and its characteristics, i.e. it 'was greatly attenuated in mice but nevertheless its gene expression was rather augmented". The specification goes on to teach, "*from the aspects of both safety and efficiency, we have been using this V- version as the vector backbone*" (Specification, paragraph bridging pages 2-3). In working examples, the specification has been using the V(-)SeV for all of the in vitro and in vivo experiments, which demonstrated SIV/Gag-specific lysis *in vitro*, detectable levels of gag expression in the respiratory tracts with the nasal swabs (table 1) that leads to high level of plasma anti-Sev antibody, but not anti-gag antibody (Specification, last paragraph, page 48). Nevertheless, when challenged with SIV, both control and vaccinated showed similar levels of plasma SIV load peaking at week 2 after the challenge (fig. 4), but the vaccinated group had significant lower viral loads after the peak, and eventually the plasma viral loads in the immunized macaques became below the detectable level, while that of the control macaques remained high (example 4). The specification goes on to teach that a CD8+ CTL response was observed in SeV/SIVgag infected cells *in vitro*, and in immunized rhesus macaques *in vivo* (examples 6-9). However, since the transgene expression level is significantly higher of V(-)SeV compared to SeV, the specification fails to teach whether the SeV could induce a protective immune response

in a mammalian subject, whether other proteins listed in claim 1 could induce a specific CTL response that would generate a protective immune response comparable to that of SIVgag. The specification fails to teach DNA vectors besides a plasmid and routes of administration besides intradermal gene gun approach could induce such an immune response, thus, the specification fails to support the full scope of the claims.

In view of the art of record, *Yu et al* (Genes Cells 1997;2:457-466) teach in disclosing the V(-)SeV, "WE HAVE SUCCEED IN CREATING A V(-)SEV WHOSE GENE EXPRESSION WAS GREATLY ENHANCED BY THE DELETION OF THE NONESSENTIAL V GENE" (abstract), they go on to teach that although the SeV could express a gp120 protein at levels that the protein could be purified, a remarkable reinforcement of expression was accomplished by the creation of V(-)SeV, which is three-fold more efficient *in vitro* compared to the SeV (column 2, page 458). Since then, the publications of record have used the V(-)SeV for investigation. It is unknown the in vivo physiological effect and the efficacy of SeV. To this end, the applicants as the skilled in the art acknowledged that there is no reason to believe the combination teachings of *Flanagan et al* or *Seth et al*, *Hurwitz et al*, and *Yu et al* would be successful because "NEITHER HURWITZ (who teaches a V(+)SeV) NOR YU DISCLOSE OR SUGGEST THAT SENDAI VIRUS WOULD BE SUITABLE AS A VACCINE VECTOR, CAPABLE OF INDUCING A PROTECTIVE, ANTIGEN-SPECIFIC, CELLULAR IMMUNE RESPONSE" (the 1st paragraph, page 24, Remarks filed 11/19/04). Although instant specification shed lights on the in vivo effect of V(-)Sev-SIV-Gag, the vaccine effect of V(+)Sev-SIV remains unknown, and unpredictable. Apparently, it is reasonable to cast doubt on the ability of sendai virus vector to induce a protective immune response. The types of the vectors are

relevant for enabling the claimed invention because each type of virus has different host range, efficacy of infection, and levels of transgene expression. *Robbins et al* (Pharmcol Ther 1998;80:35-47) teach that each type of vector system has its unique advantages and limitations, "RETROVIAL VECTORS CAN PERMANENTLY INTEGRATE INTO THE GENOME OF THE INFECTED CELL, BUT REQUIRE MITOTIC CELL DIVISION FOR TRANSDUCTION. ADENOVIRAL VECTORS CAN EFFICIENTLY DELIVER GENES TO A WIDE VARIETY OF DIVIDING AND NONDIVIDING CELL TYPES, BUT IMMUNE ELIMINATION OF INFECTED CELLS OFTEN LIMITS GENE EXPRESSION IN VIVO. HERPES SIMPLEX VIRUS CAN DELIVER LARGE AMOUNTS OF EXOGENOUS DNA; HOWEVER, CYTOTOXICITY AND MAINTENANCE OF TRANSGENE EXPRESSION REMAIN AS OBSTACLES. AAV ALSO INFECTS MANY NONDIVIDING AND DIVIDING CELL TYPES, BUT HAS LIMITED DNA CAPACITY" (abstract). In the case of the recombinant sendai virus vector, *Yu et al* clearly teach that compared to SeV, V gene deletion causes reduced infectivity but significantly more robust heterologous gene expression, thus, the V-gene deletion has apparently changed the in vivo behavior of the recombinant sendai virus. It is unpredictable how and whether the V(+)SeV could be used as a vaccine vector, and it is difficult to predict from V(-)SeV how other types of sendai virus would behave *in vivo* in the context of vaccination.

In view of the genetic vaccination art in general, it is still under development. The type of antigens, the type and efficiency of vectors, and the routes of administration are all determining factors for the outcome of the immune response mounted. In a post-filing date conference, *Moingeon et al,* (Trends Immunol 2002 Apr;23:173-5) summarized, "THE DISCOVERY OF NEW ANTIGENS ABLE TO ELICIT PROTECTIVE IMMUNE RESPONSES AGAINST INFECTIOUS PATHOGENS REMAINS ONE OF THE MOST IMPORTANT CHALLENGES IN VACCINOLOGY" (page 173, left column). "THE NEED FOR ANTIGEN-PRESENTATION PLATFORMS AND/OR ANTIGEN

FORMULATIONS ELICITING POTENT T-CELL RESPONSES AND MUCOSAL IMMUNITY IN HUMANS, AS WELL AS THE POOR PREDICTIVE VALUE OF ANIMAL MODELS, WERE EMPHASIZED ALSO". (paragraph bridging pages 174 and 175). It is unpredictable to extrapolate from the V(-)SeV to other types of sendai virus vectors.

With respect to the type of the protein, in a post-filing art, *Matano et al* (including the applicant) acknowledge that V(-)SeV/SIV-tat fails to generate the type of the protective response generated by the V(-)SeV/SIV-gag (AIDS 2003;17:1392-4). In view of such, the invention does not appear to be fully enabled in the absence of clarification of the contradictory evidence found in the references.

With respect to the routes of administration for the DNA plasmid vector, *McCluskie et al* (Mol Med 1999 May;5:287-300) teach "ROUTES OF ADMINISTRATION OF PLASMID DNA VACCINES INFLUENCES THE STRENGTH AND NATURE OF IMMUNE RESPONSES IN MICE AND NON-HUMAN PRIMATES." (See abstract) *Torres et al* (J Immunol 1997;158:4529-32) teach "TRANSFECTED CELLS IN GENE GUN-BOMBARDED SKIN, BUT NOT NEEDLE-INJECTED MUSCLE, PLAY A CENTRAL ROLE IN DNA-INITIATED AB AND CTL RESPONSE" (abstract). *Nakano et al* (J Virol 1997;71:7101-09) teach that immune reactivity with plasmid DNA encoding HCV-E2 antigenic domains is linked to the injection mode, "DIFFERENT ROUTES OF INJECTION OF HCV E2 PLASMID CAN RESULT IN QUANTITATIVELY AND QUALITATIVELY DIFFERENT HUMORAL IMMUNE RESPONSES" (see abstract). *Robbins et al* teach that non-viral vectors such as naked DNA and liposomes are inefficient in gene transfer to cell nucleus (Section 2, page 36), thus often times be delivered via gene gun intradermal approach to increase the efficiency. Apparently, vectors, whether delivered systemically or locally in vivo have unpredictable efficacy in infecting/transfecting the target cells/tissue and that it is further

unpredictable whether the transfected cells will express a therapeutic level of the heterologous gene. The specification fails to teach the effect of boosting with a plasmid other than the gene gun. It would have required undue experimentation for the skilled artisan intending to practice the instant invention.

Claims 9, 24, 37, 39 are further drawn to inoculating a DNA vector encoding the *genome* of a HIV/SIV. However, it is well known in the art, all DNA vectors particularly plasmid vectors have size limitation for foreign gene insertion, and when large amount of the foreign gene was inserted, the stability and growth potential of the plasmid is negatively linked to the size of the insertion. It is also well known in the art that the genome of the HIV/SIV is about 10,000 bps, accordingly, it is unlikely a DNA vector, particularly a plasmid vector, could carry the entire genome of SHIV, efficiently transform cells, and stably express the viral proteins. In view of such, the claims do not appear to be enabled in the absence of evidence to the contrary.

Thus, it is evident that at the time of the invention, the practitioner in the field of genetic vaccination, while acknowledging the significant potential of such therapy, still recognized that the genetic vaccination was neither routine nor accepted, and awaited significant development and guidance for its practice. Therefore, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for the claimed invention. Although the instant specification provides sufficient teaching for intranasal administration of the V(-)SeV/SIV-gag, and boost with a plasmid encoding the gag by intradermal gene gun for inducing a SIV-specific cellular response and subsequent protection of SIV infection, it is not enabled for its full scope because

determination of the effects of other components not disclosed in the specification is not predictable until they are actually made and used, hence resulting in a trial and error situation.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 7, 9, 20, 24, 26, 28-33, 37, 39, 41-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are vague and indefinite because the subject of the intranasal administration or DNA plasmid inoculation is missing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (f) he did not himself invent the subject matter sought to be patented.

Claims 1-4, 16-19 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

These claims are drawn to a subject matter that is encompassed by claims 1, 4, 5, 13 of copending Application No. 09/728,207. However, the inventive entity of this application differs from the cited application. It is unclear who is the real inventor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 16-19 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over *Nagai et al* (US application 09/728,207), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hirsch et al* (J Virol 1996;3741-52).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the

application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 1, 4, 5, 13 of the cited application is drawn to a recombinant sendai virus vector comprising a foreign gene, wherein the vector could be a DNA or RNA molecule, and the specification of the cited application teaches that sendai virus vectors have both infectivity and disseminative ability, and could be used in gene therapy for expressing any foreign gene of interest. The specification does not particularly teach a SHIV protein as the desired foreign gene of interest.

Yu et al supplemented the teaching of *Nagai et al* by establishing that it is well known in the art to use a recombinant sendai virus vector for expressing a HIV protein such as env gp120. *Yu et al* teach three different recombinant sendai virus vectors and their efficiency in expressing the gp120, wherein the V(-)SeV is the most efficient one in expressing the gp120 at a level that is comparable to vaccinia virus. *Yu et al* does not teach the particular proteins recited in claim 1.

Hirsch et al supplemented the teachings of *Nagai et al* and *Yu et al* by establishing that it is well known in the art that the env protein could be expressed together with gag and pol in a recombinant vaccinia vector and using such for SIV

vaccination, and they go on to teach a protective effect was observed in the immunized SIV-infected macaques.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vector as taught by *Nagai et al* by expressing the gp120 or gag as taught by *Yu et al* and *Hirsch et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention to use the sendai virus expressing a HIV env protein such as practiced by *Yu et al* as well as a gag protein such as taught by *Hirsch et al* because both gag and env can be expressed in a recombinant viral vector for producing an antigenic protein efficiently or served as a vaccine . Given the success as taught by *Yu et al* and *Hirsch et al,* the skilled artisan would have had a reasonable expectation of success to express SHIV proteins in a recombinant sendai virus vector. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

It is noted claim recitation "vaccine" represents the intended use of the recombinant sendai virus vector, but the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP states in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Claims 1-3, 5, 7, 9, 16-18, 20, 24, 26, 28-33, 37, 39, and 41-45 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), *Seth et al* (PNAS 1998;95:10112), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hurwitz et al* (Vaccine 1997;15:533-40); and as evidenced by *Ourmanov et al* (J Virol 2000;74:2740-51).

Amended claims are drawn to a recombinant Sendai virus vector encoding an immunodeficiency viral protein, which could be used as a vaccine to induce a protective cellular response specific to HIV/SIV.

Applicants allege that the examiner has not considered the claimed invention as a whole, nor considered the reference as a whole. Thus, the rejection is a result of piecemeal analysis and not the result of consideration of the invention as a whole. Applicants argue the *Hurwitz* did not teach a recombinant virus nor encoding a heterologous protein, *Yu et al* did not teach in vivo use of the protein, and *Flanagan et al*, *Seth et al* did not use a sendai viral vector.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, *Flanagan et al* teach using a recombinant adenovirus expressing SIV Gag protein for vaccination in mice by intranasal inoculation, and teach that mucosal route of delivery is desirable and induced a cellular immune response.

Seth et al teach using a recombinant vaccinia virus vector expressing gag-pol fusion polypeptides in multiple dosages (day 1 and 126) and inducing cytotoxic immune response specific to gag pol proteins in a rhesus monkey. Although they did not teach the sendai viral vectors, the teaching of *Yu et al* cured the deficiency. *Yu et al* supplemented the teaching of *Flanagan et al* and *Seth et al* by establishing the advantage of using V(-) sendai virus as a expression vector and its expression efficiency. *Yu et al* further compared the V- SeV with the *vaccinia virus* that was used by *Seth*, and teach "THE V(-) VERSION APPEARS TO BE EXCELLENT AND ALMOST COMPARABLE TO THE ABOUVE NOTED VV-BASED EXPRESSION" (column 1, page 462, emphasis added). Clearly, *Yu et al* teach that sendai virus could be used as a carrier for expressing a nonanalogous viral protein, such as the immunodeficiency virus, in place of the vaccinia virus or interchangeably with other known viral vectors. Some of the advantages of a V(-)SeV as listed in page 16 of the remarks are taught by *Yu et al* such as the robust heterologous gene expression capability in mammalian cells, moderate pathogenesis, and broad host range. Other advantage such as non-pathogenic in primates (d) is also known in the art such as taught by *Hurwitz et al* (e.g. the abstract). *Hurwitz et al* also teach the feasibility of intranasal multiple inoculation of a Sendai virus in primates (abstract, figures 1-4, and table 1). *Hurwitz et al* go on to teach the advantage of using Sendai virus as a potential human vaccine because its long-lasting effect stimulating memory B-cells as well as CTL response (last paragraph, page 539). Applicants argue that Hurwitz et al use a wild type sendai virus, not a recombinant one, it is noted that majority of recombinant viral vectors inherently possess the characteristics of the virus from which they are derived,

and Yu et al has taught that the recombinant V(-)SeV differs from the SeV in reduced infectivity, and increased level of transgene expression.

Applicants also argue it is not known what type of immune response the sendai virus vector encoding a SHIV protein would induce, it is noted the nature of an immune response is predominantly determined by the type of antigens presented to the antigen presenting cells. For example, both the AdV-gag of *Flanagan et al* and the VV-gag-pol of *Seth et al* induced a long-live cellular immune response to HIV Gag, even though applicants allege that the adenovirus vector used by *Flanagan et al* is less efficient compared to instant invention. Thus, the skilled in the art would have had a reasonable expectation to induce a cellular immune response using the vector disclosed by *Yu et al* for *in vivo* expression of *Gag* since *Yu et al* teach the expression levels of the V(-)SeV is comparable to that of the VV).

Applicants then argue the combined teachings did not show that a protective immune response against SHIV infection. *Ourmanov et al* evidenced that VV-gag-pol vaccine (as used by *Seth et al*) indeed provided protection from high levels of viremia and AIDS following challenge with a pathogenic strain of SIV in macaques. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.

See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, all of the references relied on are prior art of record teaching the level of ordinary skill at the time the claimed invention was made.

In response to applicant's argument that there are no specifically articulated rationale and evidentiary support for the motivation to combine the reference, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, it is well known in the art that certain HIV proteins such as the gag and gag-pol fusion could induce a long-lasting humoral and cellular response, and modifying/reducing viral load in the infected subject when expressed with more than one type of viral vectors such as adenoviral vector and vaccinia vector as taught by

Flanagan et al and *Seth et al*, it is also well known in the art that V(-) sendai viral vector is capable of expressing a HIV protein at a level comparable to the VV vector, and other advantages as taught by *Hurwitz et al*, and *Yu et al*. Even though *Hurwitz et al* used a strain of wild type sendai virus, it is known that the deletion of the V gene further enhanced the ability for the recombinant viral vector to express a heterologous gene as taught by *Yu et al* and is safer than the wild type virus. These teachings would reasonably suggest to the skilled artisan that one can use different type of viral vectors for expressing a HIV/SIV protein and using such for vaccination with a reasonable expectation of success. Note that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al* or *Seth et al*, in view of *Hurwitz et al*, and *Yu et al* by substituting and/or combining the recombinant adenoviral or vaccinia vector with a recombinant Sendai viral vector and delivering such via intranasal inoculation with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention given the numerous carrier vectors known in the art, and all proven to be effective in expressing a viral protein at sufficient levels. Thus, it falls within the bound of optimization for the skilled artisan to determine which vector would serve their goal the best.

Applicants argue that there is no suggestion in the cited references that why one would substitute the adenoviral or vaccinia viral vector with a sendai viral vector. In response, the fact that the skilled artisan use different types of recombinant viral vectors expressing SHIV proteins such as taught by *Flanagan et al* (rbAdV-gag), *Yu et al* (rbSeV-env), or *Seth et al* (rbVV-gag-pol), demonstrated there must be some motivation to do so. To this end, the court has determined "AN EXPRESS SUGGESTION TO SUBSTITUTE ONE EQUIVALENT COMPONENT OR PROCESS FOR ANOTHER IS NOT NECESSARY TO RENDER SUCH SUBSTITUTION OBVIOUS". *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Above said, the Examiner acknowledges that the vector used for expressing a certain antigen does play a role in the nature and intensity of the immune response upon *in vivo* administration, thus, the arguments of (a) and (c) of page 16 are considered persuasive because it may not predictable whether the V(-) SeV/SIV-Gag could elicit a protective effect against subsequent SIV challenge. However, the current claims encompass any SeV, any SHIV protein listed in claim 1, and boosting with any DNA by any route of inoculation, and a DNA encoding HIV/SIV genome. The unexpected results do not apply to those elements. The court has determined, "WHETHER THE UNEXPECTED RESULTS ARE THE RESULT OF UNEXPECTEDLY IMPROVED RESULTS OR A PROPERTY NOT TAUGHT BY THE PRIOR ART, THE "OBJECTIVE EVIDENCE OF NONOBVIOUSNESS MUST BE COMMENSURATE IN SCOPE WITH THE CLAIMS WHICH THE EVIDENCE IS OFFERED TO SUPPORT." IN OTHER WORDS, THE SHOWING OF UNEXPECTED RESULTS MUST BE REVIEWED TO SEE IF THE RESULTS OCCUR OVER THE ENTIRE CLAIMED RANGE. *IN RE CLEMENS*, 622 F.2D 1029, 1036, 206 USPQ 289,

296 (CCPA 1980)" ((MPEP 716.02(d), emphasis added)). Accordingly, until the claims are limited to the scope of the unexpected results, the rejection stands.

Claims 11-13 and 15 stand rejected and the rejection has been modified under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS).

Applicants argue that the combined teachings in this rejection are similarly flawed for reasons given above, which have been addressed *supra*.

Applicants then argue that the Examiner has overlooked select claim limitations in step b, which require contacting the APC with a Th cell and cytotoxic T cell.

The arguments have been fully considered but found not persuasive because this limitation has been addressed in the Office action mailed 1/13/03.

Claim 11 and dependent claims are drawn to a standard CTL assay, which is taught by both *Flanagan et al* and *Kast et al.*

Flanagan et al teach the *in vitro* CTL assay, wherein a recombinant viral vector encoding a gag protein is introduced to APCs (splenocytes, stimulator cells), which then incubated (contact) with splenocytes of immunized mice, which splenocytes comprise T helper and T cytotoxic cells (responders), and a cellular immune response specific to a SIV gag is induced (CTL-assays, page 992).

The method of *Flanagan et al* differs from instant claimed in that they did not use a sendai viral vector expressing the HIV/SIV protein, *Yu et al* supplemented the

teachings of *Flanagan et al* by establishing it is well known in the art to use a sendai viral vector to express an immunodeficiency virus protein at a high level. It would have been obvious for the skilled in the art to use one of the art known vectors in the CTL assay with a reasonable expectation of success.

The teaching of *Kast et al* supplemented the *Flanagan et al* by establishing the infectivity of the sendai virus in antigen-presenting cells. *Kast et al* extensively discussed how to use the sendai virus infected dendritic cells (APC) in the CTL assay to measure an in vivo immune response (left column, page 3187), to test the activity of T helper and cytotoxic T lymphocytes.

It is noted each CTL assay in the cited references may slightly differ in the type of antigen presenting cells, the source of Th and Tcytotoxic cells, but these are the obvious alternatives and variants well known to the ordinary skilled in the art.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al* and *Kast et al*, by employ the vector taught by *Yu et al* with a reasonable expectation of success in inducing a specific cellular immune response. The ordinary skilled artisan would have been motivated to modify the method for their particular needs of investigation, i.e. a particular disease of interest, or a particular antigen of interest, etc. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS) as applied to claims 11-13, and 15 above, further in view of *Boutillon et al* (US 6,015,564).

Claim 14 is drawn to using an autologous herpesvirus papio-immortalized B lymphoblastoid cell as the APC.

Applicants argue that the combined teachings in this rejection are similarly flawed for reasons given above, which have been addressed *supra*.

Applicants then argue even if the references were combined as suggested, one would not arrive at the claimed invention because Boutillon teach using HSV transforming B lymphoid cells, the disclosure does not cure the deficiencies of *Flanagan et al, Yu,* and *Kast et al* in terms of using sendai virus as a carrier for inducing a cellular immune response either in vitro or in vivo.

As an initial matter, applicants are reminded that these claims are drawn exclusively to *in vitro* experiments, the desired results are much easier to achieve because the reaction conditions could be control and adjust with greater ease. Given the success taught by both *Flanagan et al* and *Kast et al* of inducing a cellular immune response to HIV-gag and sendai virus, and given the expression efficiency of the V(-) SeV taught by *Yu et al*, the skilled artisans would have had a reasonable expectation of success of inducing a cellular immune response *in vitro* using the sendai virus of *Yu et al* for expressing the gag protein.

Boutillon et al supplemented the teachings of *Flanagan et al* and *Kast et al* by establishing the well-known status in the art for using transforming B lymphoblastoid cells to make an immortalized cell line for CTL assay. It is the combined teachings as a whole that teaches the claimed invention.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al, Yu et al, Kast et al*, by employ immortalized cells as taught by *Boutillon et al* in the CTL response as taught in the combined teachings of *Flanagan et al, Yu et al, Kast et al* with a reasonable expectation of success in inducing a specific cellular immune response. The ordinary skilled artisan would have been motivated to modify the method because the immortalized cells would be easier to care for. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 16-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 5, 13 of copending Application No. 09/728,207 in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hirsch et al* (J Virol 1996;3741-52).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of present application and the claims 1, 4, 5, 13 of the cited patent application are each drawn to a recombinant sendai viral vector carrying a foreign gene.

The claims of the present application and the cited patent differ one from the other in that claims of the cited patent application does not particularly recite the proteins of instant claim 1. However, before the effective filing date of the instant application, *Yu et al* teach using a recombinant sendai virus for expressing the env gp120 of SHIV, and *Hirsch et al* teach that it is well known in the art that the env protein could be expressed together with gag and pol in a recombinant vaccinia vector and using such for SIV vaccination, and they go on to teach a protective effect was observed in the immunized SIV-infected macaques.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the vector as taught by *Nagai et al* (instant application) for expressing the gp120 as practiced by Yu et al or for expressing other SHIV proteins such as gag as taught by *Hirsch et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention to use the recombinant sendai virus vector expressing a HIV protein because

each viral vector has its own advantage and disadvantage, and both gag and env can be expressed in a recombinant viral vector for producing an antigenic protein efficiently or served as a vaccine. Given the success as taught by *Yu et al* and *Hirsch et al*, the skilled artisan would have had a reasonable success to express SHIV proteins in a recombinant sendai virus vector. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Accordingly, the claimed vectors in the copending and the present application are obvious variants.

This is a provisional obviousness-type double patenting rejection.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Ram R. Shukla** can be reached on 571-272-0735. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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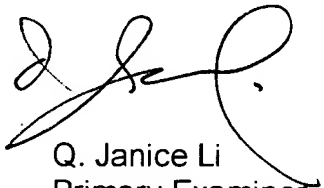

Q. Janice Li
Primary Examiner
Art Unit 1632

QJL
January 21, 2005

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